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Substitute for form 1449A/B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Application Number	10/616,046
Sheet	1	of	5	Filing Date	July 8, 2003
				First Named Inventor	Mladen MERCEP
				Art Unit	TBA
				Examiner Name	TBA
				Attorney Docket Number	03818/100L652-US1

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
1.	6,297,260	10/02/2001	Bandarage et al.		
2.	4,710,495	12/01/1987	Bodor		
3.	6,402,733	06/11/2002	Daugherty		
4.	6,273,086	08/14/2001	Ohki et al.		
5.	6,228,346	05/08/2001	Zhang et al.		
6.	5,747,467	05/05/1988	Agouridas et al.		
7.	4,474,768	10/02/1984	Bright		

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
8.	WO 94/13690	✓	06/23/1992	Rhone-Poulenc Rorer Limited	
9	WO 94/14834	✓	07/07/1994	Rhone-Poulenc Rorer Limited	
10.	WO 92/13873	✓	08/20/1992	Aktiebolaget Astra	
11.	WO 92/13872	✓	08/20/1992	Aktiebolaget Astra	
12.	WO 00/42055	✓	07/20/2000	Zambon Group S.P.A.	
13.	EP 0283055	✓	08/29/1990	Sour Pliva farmaceutska	
14.	EP 0775489	✓ -	05/28/1997	Taisho Pharmaceutical Co. Ltd.	
15.	EP 0771564	✓ -	05/07/1997	Taisho Pharmaceutical Co. Ltd.	
16.	WO 97/41255	✓	11/06/1997	Massachusetts Institute of Technology	
17.	EP 00680967	✓	10/14/1998	Hoechst Marion Roussel	
18.	WO 99/51616	✓	10/14/1999	Pliva, Farmaceutska	
19.	EP 0984019	✓ -	03/08/2000	Pfizer Products Inc.	
20.	WO 98/56801		12/17/1998	Pfizer Products Inc.	
21.	WO 94/14834	✓ -	07/07/1994	Rhone-Poulenc Rorer Limited	
22.	EP 0984019 A1		03/08/2000	Pfizer Products Inc.	
23.	WO 98/56801	✓ -	12/17/1998	Pfizer Products Inc.	

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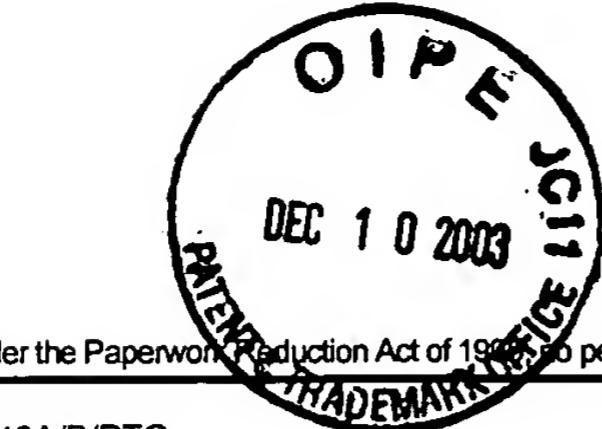
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NON PATENT LITERATURE DOCUMENTS						
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.				T ²
	24. ✓	Gladue R. P. et al., "In Vitro and In Vivo Uptake of Azithromycin (CP-62,993) by Phagocytic Cells: Possible Mechanism of Delivery and Release at Sites of Infection," <i>Antimicrob. Agents and Chemother.</i> , 33, 1989, 277-282				
	25.	Olsen K. M. et al., "Intrapulmonary Pharmacokinetics of Zithromycin in Healthy Volunteers Given Five Oral Doses," <i>Antimicrob. Agents and Chemother.</i> , 40, 1996, 2582-2585				
	26.	Mikasa, K. et al., "The anti-inflammatory effect of erythromycin in zymosan-induced peritonitis of mice," <i>J. Antimicrob. Chemother.</i> , 30, 1992, 339-348				
	27.	"Discussion, Genomic organization of axolotl 1g genes," <i>J. Immunol.</i> , 159, 1997, 3395-4005				
	28.	Takizawa, H. et al., "Erythromycin Modulates IL-8 Expression in Normal and Inflamed Human Bronchial Epithelial Cells," <i>Am. J. Respir. Crit. Care Med.</i> , 156, 1997, 266-271				
	29.	Labro, M.T., "Anti-inflammatory activity of macrolides: a new therapeutic potential?" <i>J. Antimicrob. Chemother.</i> , 41, 1998, 37-46				
	30. *	Cazzola, M., et al., "Potential role of macrolides in the treatment of asthma," <i>Mondaldi Arch. Chest Dis.</i> , 55, 2000, 231-236				
	31. ✓	Avila, P.C. et al., "Macrolides, asthma, inflammation, and infection," <i>Ann. Allergy Asthma Immunol.</i> , 84, 2000, 565-568				
	32.	Amayasu, H. et al., "Clarithromycin suppresses bronchial hyperresponsiveness associated with eosinophilic inflammation in patients with asthma," <i>Ann. Allergy, Asthma & Immunol.</i> , 84, 2000, 594-598				
	33.	Shoji, T. et al., "Anti-inflammatory effect of roxithromycin in patients with aspirin-intolerant asthma," <i>Clin. Exp. Allergy</i> , 29, 1999, 950-956				
	34.	Griffith, E.C., et al., "Yeast Three-Hybrid System for Detecting Ligand-Receptor Interactions," <i>Methods in Enzymology</i> , 328m 2000, 89-110				
	35.	Denis A. et al., "Synthesis and Antibacterial Activity of HMR 36K47, A New Ketolide Highly Potent Against Erythromycin-Resistant and Susceptible Pathogens," <i>Bioorg. & Med. Chem. Lett.</i> , 9, 1999, 3075-3080				
	36.	Agouridas C. et al., "Synthesis and Antibacterial Activity of Ketolides (6-O-Methyl-3-oxoerythromycin Derivatives): A New Class of Antibacterials Highly Potent against Macrolide-Resistant and -Susceptible Respiratory Pathogens," <i>J. Med. Chem.</i> , 41, 1998, 4080-4100				
	37.	Sun, Or Y. et al. <i>J. Med. Chem.</i> 2000, 43, 1045-1049				
	38.	McFarland, J. W. et al., "Repromycin Derivatives with Potent Antibacterial Activity against <i>Pasteurella multocida</i> ," <i>J. Med. Chem.</i> , 50, 1997, 1041-1045				
	39.	Denis A. et al., "Synthesis of 6-O-Methyl-Azithromycin and Its Ketolide Analogue via Beckmann Rearrangement of 9(E)-6-O-Methyl-Erythromycin Oxime," <i>Bioorg. & Med. Chem. Lett.</i> , 8, 1998, 2427-2432				
	40.	Lartey et al., "Synthesis of 4"-Deoxy Motilides: Identification of a Potent and Orally Active Prokinetic Drug Candidate," <i>J. Med. Chem.</i> , 38, 1998, 1793-1798				

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41.	Kirst, H.A. et al., "34. Metabolism of macrolides," Bryskier, A. J. et al., Ed. <i>Macrolides, Chemistry, Pharmacology and Clinical Use</i> ; Bryskier, Arnette Blackwell: Paris, 1993; pp 485-491
42.	Ma, Z. et al., "Discovery and Development of Ketolides as a New Generation of Macrolide Antimicrobial Agents," <i>Current Medicinal Chemistry - Anti-Infective Agents</i> , 1, 2002, 15-34
43.	Pascual A. et al., "Uptake and intracellular activity of ketolide HMR 3647 in human phagocytic and non-phagocytic cells," <i>Clin. Microbiol. Infect.</i> , 7, 2001, 65-69
44.	Hand, W. L. et al., "Characteristics and mechanisms of azithromycin accumulation and efflux in human polymorphonuclear leukocytes," <i>Int. J. Antimicrob. Agents</i> , 18, 2001, 419-425
45.	Amsden, G. W., "Advanced-generation macrolides: tissue-directed antibiotics," <i>Int. J. Antimicrob. Agents</i> , 18, 2001, 11-15
46.	Johnson, J. D. et al., "Antibiotic uptake by alveolar macrophages," <i>J. Lab. Clin. Med.</i> , 95, 1980, 429-439
47.	Wildfeuer, A. et al., "Uptake of Azithromycin by Various Cells and Its Intracellular Activity under In Vivo Conditions," <i>Antimicrob. Agents Chemother.</i> , 40, 1996, 75-79
48.	Scorneaux, B. et al., "Intracellular Accumulation, Subcellular Distribution, and Efflux of Tilmicosin in Chicken Phagocytes," <i>Poult. Sci.</i> , 77, 1998, 1510-1521
49.	Mtairag, E. M. et al., "Investigation of dirithromycin and erythromycylamine uptake by human neutrophils <i>in vitro</i> ," <i>J. Antimicrob. Chemother.</i> 33, 1994, 523-536
50.	Anderson R. et al., "An in-vitro evaluation of the cellular uptake and intraphagocytic bioactivity of clarithromycin (A-56268, TE-031), a new macrolide antimicrobial agent," <i>J. Antimicrob. Chemother.</i> , 22, 1988, 923-933
51.	Tasaka, Y. et al., "Rokitamycin Uptake by Alveolar Macrophages," <i>Jpn. J. Antibiot.</i> 41, 1988, 836-840
52.	Harf, R. et al., "Spiramycin uptake by alveolar macrophages," <i>J. Antimicrob. Chemother.</i> , 22, 1988, 135-140
53.	Suzuki, T. et al., "General and facile method for determination of configuration of steroid-17-yl-methyl glycolates at C-20 based on kinetic examination," <i>Chem. Soc., Perkin Trans. 1</i> , 1998, 3831-3836
54.	McLean, H.M. et al., "Novel Fluorinated Antiinflammatory Steroid with Reduced Side Effects: Methyl 9 α -Fluoroprednisolone-16-carboxylate," <i>J. Pharm. Sci.</i> 1994, 83, 476-480
55.	Little, R.J. et al., "Soft Drugs Based on Hydrocortisone: The Inactive Metabolite Approach and Its Application to Steroidal Antiinflammatory Agents," <i>Pharm. Res.</i> , 16, 1999, 961-967
56.	Kertesz, D.J. et al., "Thiol Esters from Steroid 17 β -Carboxylic Acids: Carboxylate Activation and Internal Participation by 17 α -Acylates," <i>J. Org. Chem.</i> , 51, 1986, 2315-2328
57.	Phillipps, G. et al., "Synthesis and Structure - Activity Relationships in a Series of Antiinflammatory Corticosteroid Analogues, Halomethyl Androstane-17 β -carbothioates and 17 β -carbofelenoates," <i>J. Med. Chem.</i> 37, 1994, 3717-3729
58.	Bright, G.M. et al., "Synthesis, In Vitro and In Vivo Activity of Novel 9-Deoxo-9a-AZA-9a-Homoerythromycin A Derivatives; A new Class of Macrolide Antibiotics, the Azalides" <i>J. Antibiot.</i> , 41, 1998, 1029-1047
59.	Costa, A.M. et al., "Hybrids of macrolides and nucleobases or nucleosides," <i>Tetrahedron Letters</i> , 41, 2000, 3371-3375

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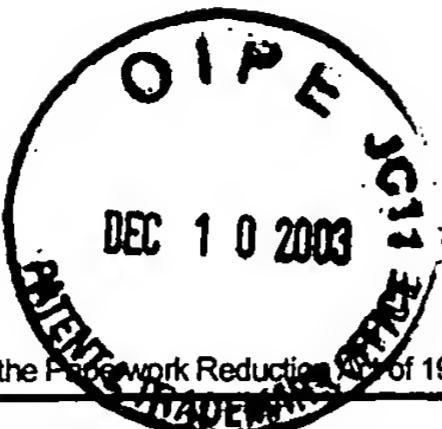
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60.	Newman, S.P. et al., "Evaluation of jet nebulisers for use with gentamicin solution," <i>Thorax</i> , 40, 1985, 671-676
61.	Berenberg, M.J. et al., "Comparison of Metered-Dose Inhaler Attached to an Aerochamber with an Updraft Nebulizer for the Administration of Metaproterenol in Hospitalized Patients," <i>J. Asthma USA</i> , 22, 1985, 87-92
62.	Warner, Timothy D. et al., "Nonsteroid drug selectivities for cyclo-oxygenase -1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: A full in vitro analysis," <i>Proc. Natl. Acad. Sci. USA</i> 96, June 1999, 7563-7568
63.	Luong, Brigitte T. et al., "Treatment Options for Rheumatoic Arthritis: Celecoxib, Leflunomide, Etanercept, and Infliximab," <i>The Annals of Pharmacotherapy</i> 34, 2000, 743-760
64.	Taketo, Makoto M., "Cyclooxygenase-2 Inhibitors in Tumorigenesis (Part II)," <i>Journal of the National Cancer Institute</i> 90, 21, 1998, 1609-1620
65.	Fournier, David B. et al., "COX-2 and Colon Cancer: Potential Targets for Chemoprevention," <i>Journal of Cellular Biochemistry Supplement</i> 34, 2000, 34-97
66.	Carswell, E.A. et al., "An endotoxin-induced serum factor that causes necrosis of tumors," <i>Proc. Nat. Acad. Sci. USA</i> 72, 9, 1975, 3666-3670
67.	Elliott, Michael J. et al., "Randomised double-blind comparison of chimeric monoclonal antibody to tumour necrosis factor α (cA2) versus placebo in rheumatoid arthritis," <i>The Lancet</i> 344, 1994, 1005-1110
68.	Mori, Lucia et al., "Attenuation of Collagen-Induced Arthritis in 55-kDa TNF Receptor Type 1 (TNFR1)-IgG1-Treated and TNFR1-Deficient Mice," <i>Journal of Immunology</i> , 1996, 3178-3182
69.	Pfeffer, Klaus et al., "Mice Deficient for the 55 kd Tumor Necrosis Factor Receptor Are Resistant to Endotoxic Shock, yet Succumb to <i>L. monocytogenes</i> Infection," <i>Cell</i> 73, 1993, 457-467
70.	Georgopoulos, Spiros et al., "Transmembrane TNF Is Sufficient To Induce Localized Tissue Toxicity and Chronic Inflammatory Arthritis in Transgenic Mice," <i>Journal of Inflammation</i> 46, 1996, 86-97
71.	Keffer, Jeanne et al., "Transgenic mice expressing human tumour necrosis factor: a predictive genetic model of arthritis," <i>The EMBO Journal</i> 10, 13, 1991, 4025-4031
72.	Van Assche, Gert et al., "Anti-TNF agents in Crohn's disease," <i>Exp. Opin. Invest. Drugs</i> , 2000, 103-111
73.	Romo, Daniel et al., "Total Synthesis and Immunosuppressive Activity of (-)-Pateamine A and Related Compounds: Implementation of a β -Lactam-Based Macrocyclization," <i>J. Am Chem. Soc.</i> 120, 1998, 12237-12254
74.	Huang, Chun-Ming et al., "Targeting delivery of paclitaxel into tumor cells via somatostatin receptor endocytosis," <i>Chemistry & Biology</i> 7, 9, 2000, 453-461
75.	Pandor, Mark W. et al., "Photochemical Control of the Infectivity of Adenoviral Vectors Using a Novel Photocleavable Biotinylation Reagent," <i>Chemistry & Biology</i> 9, 2002, 567-573
76.	Colliet, H.O.J. et al., "The Abdominal Constriction Response and Its Suppression by Analgesic Drugs in the Mouse," <i>Br. J. Pharmac. Themoth.</i> 32, 1968, 295-310
77.	Fukawa, Kazunaga et al., "A Method for Evaluating Analgesic Agents in Rats," <i>Journal of Pharmacological Methods</i> 4, 1980, 251-259

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78.	Schweizer, A. et al., "Combined automated writhing/motility test for testing analgesics," <i>Agents and Actions</i> 23, 1/2, 1988, 29-31
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.

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